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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,836	03/30/2006	Angelo Guglielmotti	281760US0PCT	6824
22850	7590	05/25/2010	EXAMINER	
OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, L.L.P. 1940 DUKE STREET ALEXANDRIA, VA 22314				RAMACHANDRAN, UMAMAHESWARI
ART UNIT		PAPER NUMBER		
1627				
NOTIFICATION DATE			DELIVERY MODE	
05/25/2010			ELECTRONIC	

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RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ANGELO. GUGLIELMOTTI, LORENZO POLENZANI,
ALESSANDRA ALISI, and NICOLA CAZZOLLA

Appeal 2009-007941
Application 10/560,836
Technology Center 1600

Oral Hearing Held: April 22, 2010

Before ERIC B. GRIMES, JEFFREY N. FREDMAN, and
STEPHEN WALSH, *Administrative Patent Judges*.

APPEARANCES:

ON BEHALF OF THE APPELLANT:

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1 The above-entitled matter came on for hearing on Thursday, April 22,
2 2010, commencing at 2:00 p.m., at the U.S. Patent and Trademark Office,
3 600 Dulany Street, Alexandria, Virginia, before Paula Lowery, Notary
4 Public.

5 THE CLERK: Good morning. Calendar Number 71, Appeal No. 2009-
6 007941, Mr. Cunningham.

7 JUDGE GRIMES: Good afternoon, Mr. Cunningham.

8 MR. CUNNINGHAM: Good afternoon.

9 JUDGE GRIMES: You have 20 minutes to present your case. You can get
10 started whenever you're ready.

11 MR. CUNNINGHAM: I won't reiterate our basic argument, however, I'd
12 like to make a point with regard to the Jorum reference.

13 The Jorum reference, which was applied in all the obviousness rejections,
14 does not disclose the compound of Formula 1 that is required to practice the
15 method of the invention, nor does it disclose the use of 5-HT4 antagonists to
16 treat neuropathic pain.

17 The only references that teach the compound in Formula 1 do not in any way
18 refer to treatment of neuropathic pain, so we're dealing with completely
19 different sets of patients here or subjects.

20 Subjects with neuropathic pain, as opposed to the prior art subjects in the
21 primary references, are subjects that have no susceptible pain.

22 Therefore, while Jorum and the primary references all fall within a similarly
23 broadly defined field with regard to pain, they're not analogous in the sense
24 that they teach different compounds and they teach different groups of
25 subjects to be treated.

1 In fact, the Jorum reference does not teach the 5-HT4 antagonist at all. It
2 teaches a different process of chemical compounds that interact with the
3 opioid receptor.

4 The Examiner's obviousness rejections are premised on a faulty syllogism
5 that any disease exhibiting the symptom of allodynia, whether it's
6 nociceptive allodynia or allodynia associated with neuropathic pain, can be
7 treated with a 5-HT4 antagonist.

8 Therefore, according to the Examiner, the neuropathic pain associated with
9 the symptoms of allodynia or hyperalgesia can be treated with a 5-HT4
10 antagonist.

11 JUDGE WALSH: A question about allodynia. Gaster teaches that
12 compounds of their Formula 1 can be used to treat migraines, and in the
13 exhibits that are attached to the Brief in the evidence appendix, there is an
14 exhibit on allodynia. That exhibit says allodynia is a clinical feature of
15 many pain conditions, such as migraine, post-herpetic neuralgia and others.
16 Does that exhibit mean that migraine is associated with allodynia because
17 allodynia is a clinical feature of migraines? If Gaster's teaching treats
18 migraines, why isn't that the same as treating allodynia?

19 MR. CUNNINGHAM: Allodynia is a symptom. It's not the disease itself.
20 Neuropathic pain has different structures associated with the generation and
21 origin of the neuropathic pain. In other words, injury to the nerves, whereas
22 Gaster is referring to multiceptive pain.

23 Now, allodynia can be a symptom of either a nociceptive diseases or
24 disorders taught by Gaster, or it can also be a symptom of neuropathic pain.

1 JUDGE WALSH: There is a dependent claim that says wherein the patients
2 of Claim 6 have allodynia. So is that a subset of patients being treated in
3 Claim 6? If so, is it a subset that's fairly reflected by Gaster's disclosure?

4 MR. CUNNINGHAM: No, it would not be fairly reflective of Gaster
5 because the claims require treatment of a subject that has neuropathic pain,
6 which is caused by damaged nerves. Whereas the Gaster patients are under
7 a completely different group associated with conditions exhibiting
8 nociceptive pain.

9 JUDGE FREDMAN: Isn't allodynia pretty much a well-recognized feature
10 of neuropathic pain?

11 MR. CUNNINGHAM: According to the references cited by the Examiner,
12 it is a symptom of some types of neuropathic pain. It's not necessarily
13 completely characteristic of neuropathic pain, but it can be one symptom of
14 that.

15 JUDGE WALSH: One more area I'd like you to talk about, again relating to
16 Gaster's disclosure of treating migraine.

17 In another of the exhibits that is attached to the Brief, there's an article on
18 migraine; and it says under the heading pathophysiology, "Current thinking
19 is that a phenomena known as cortical spreading depression is responsible
20 for migraine."

21 Is cortical spreading depression a condition that's associated with
22 neuropathic pain?

23 MR. CUNNINGHAM: I'm not an expert on that particular point. However
24 --

25 JUDGE FREDMAN: The definition, according to the ISP, is pain initiated
26 or caused by a lesion of the nervous system.

1 This reference seems to say that we have -- the neuro imaging techniques
2 which appear to show migraine is primarily a disorder of the brain
3 neurologically, not of the blood vessels.

4 The implication of that definition, in concert with this path of physiology, is
5 that migraine itself, at least in part, is a form of neuropathic pain.

6 MR. CUNNINGHAM: I don't believe that Gaster says that migraine is a
7 form of neuropathic pain.

8 JUDGE FREDMAN: No, we're not providing Gaster to say that. This is
9 migraine from Wikipedia, which -- did they submit?

10 JUDGE WALSH: Yes, this was submitted as part of the evidence appendix.

11 JUDGE FREDMAN: So Gaster himself teaches that migraine, obviously, is
12 treated with this compound.

13 The question is: is migraine itself a neuropathic disease or not? Given the
14 definition neuropathic pain in this type of physiology, there's a suggestion at
15 least of a tight connection between migraine and neuropathic pain.

16 MR. CUNNINGHAM: The Bernstein reference, which was cited in the
17 second issue, refers to the migraine. Refers to a number of migraine
18 syncretization factors on pages 1706 and 1707, and various potential
19 mechanisms of generation of pain and migraine.

20 However, it does not in any way correlate migraine with neuropathic pain or
21 nerve damage. In fact, the Bernstein reference actually teaches away from the
22 Examiner's arguments because on page 1707 --

23 JUDGE FREDMAN: Does Bernstein actually talk about the actual path of
24 physiology, or about the triggers that cause migraine? That's different than
25 what's actually happening in the Brief, right?

1 Presumably, with migraine something is happening in the brain to cause the
2 migraine, right? There's a trigger that causes that, but it's the
3 pathophysiology that determines whether it's neuropathic or not, not the
4 trigger. The trigger is simply whatever cause is inducing that
5 pathophysiology.

6 MR. CUNNINGHAM: I think the distinction that I'd like to make is that the
7 prior art that's been applied here does not indicate that migraine is caused by
8 some damage to the nerves. It could be, you know, the mechanism or the
9 triggers that are disclosed by Bernstein, for instance, which we regard as
10 various mechanisms.

11 Bernstein at 1706 the second column indicates since it is peripheral
12 nociceptors and various sensitivities to other neurons may be associated as
13 triggers to migraine. However, it doesn't correlate these to neuropathic pain.
14 Did I make that distinction?

15 JUDGE FREDMAN: I hear the distinction you're making.

16 JUDGE GRIMES: I have a different question. It seems to me that the
17 Examiner's rationale for combining Gaster, Smith and Jorum is that Gaster
18 teaches the compounds that are in your claims and says they're 5-HT4
19 receptor antagonists.

20 Smith teaches that a different compound having the same activity potentiates
21 the treatment with a different compound for allodynic pain.

22 Jorum teaches that allodynia is a frequent symptom in neuropathic pain.
23 Therefore, it would be obvious to treat the allodynia and neuropathic pain
24 with a 5-HT4 receptor antagonist, like the one taught by Gaster, in
25 combination with this other compound.

26 What's wrong with that rationale?

1 MR. CUNNINGHAM: The symptom of allodynia associated with
2 neuropathic pain is distinct because it has a different origin.
3 JUDGE GRIMES: How does this differ from teaching inflammation
4 resulting from one thing and inflammation resulting from another? You're
5 still treating the symptom, right? You're treating the inflammation.
6 In the Examiner's reasoning, you're treating the symptom of allodynia, and
7 the treatment is going to be the same regardless of the cause of allodynia.
8 Do we have any evidence that allodynia has to be treated differently
9 depending on what causes it?
10 MR. CUNNINGHAM: Well, I don't think prior art establishes that the
11 allodynia associated with neuropathic pain has the same origin or the same
12 cause.
13 It would have a different origin because it's associated with nerve damage,
14 whereas the allodynia -- for instance, intestinal allodynia is caused by the
15 stimulation of the intestines by the balloon that's used in the experimental
16 model.
17 JUDGE GRIMES: Granted, but where's the evidence that the difference in
18 cause requires a difference in treatment? That's my question.
19 MR. CUNNINGHAM: I think it's the Examiner's burden to indicate that the
20 allodynia associated with neuropathic pain has the same origin and would be
21 treated in the same way that you would treat other diseases that exhibit that
22 symptom.
23 It's worth noting that the claims are directed to treatment of neuropathic
24 pain, not to the treatment of allodynia; and not to the treatment of --
25 JUDGE GRIMES: But if you're treating a patient with neuropathic pain,
26 even if you're treating a symptom not the underlying cause of the symptom,

1 aren't you still treating the patient?

2 MR. CUNNINGHAM: Well, there's no expectation that treatment with the
3 compounds required by the claim of Formula 1 would have any effect at all
4 on neuropathic pain, or on allodynia associated with neuropathic pain.

5 I'd like to make sure I'm clearly distinguishing between the disease and the
6 symptoms. The symptoms of allodynia can be exhibited by nociceptive
7 disorders or by neuropathic disorders.

8 However, as indicated in the specification, the treatment of neuropathic pain
9 originating from nerve damage is quite difficult, and drugs that work for
10 treating nociceptive pain conditions, including symptoms like allodynia,
11 don't necessarily work for neuropathic pain because of the different origin of
12 the pain.

13 One is associated with structural damage to the nervous system. The other is
14 associated with stimulation of nociceptive receptors.

15 JUDGE GRIMES: Where does the spec talk about different compounds
16 being required? Different treatments being required for the different kinds
17 of pain?

18 MR. CUNNINGHAM: Page 2, line 10 of the specification indicates that
19 neuropathic pain is notoriously difficult to treat; and I would refer the
20 Board's attention to the background section.

21 There are also some in the reference to Bernstein applied by the Examiner.

22 There are also teachings away from using 5-HT antagonist to treat migraine.

23 In fact, page 1707 at the bottom of the second column indicates that
24 migraine can be treated with agonist to this 5-HT if not antagonist.

25 JUDGE WALSH: That is page 1707?

26 MR. CUNNINGHAM: Page 1707 at the bottom of the second column.

1 JUDGE GRIMES: Of course, that's a different class of compounds than the
2 ones in Gaster. Gaster is 5-HT4, this is 5-HT1-b, 1-d.

3 MR. CUNNINGHAM: Gaster does refer to 5-HT4, but they're in the same
4 family. Also, Jorum teaches opioid receptor drugs that stimulate the opioid
5 receptor. It doesn't have anything to do with serotonin or 5-HT receptors as
6 Gaster.

7 So the distinction I'd like to make, again, is Jorum is not analogous art
8 because it doesn't teach the compound. It teaches you can use an opioid
9 compound to treat the neuropathic pain.

10 However, the other references that do teach the 5-HT4 or the compounds of
11 Formula 1 don't teach treating the class of subjects that have neuropathic
12 pain.

13 JUDGE WALSH: If the Examiner relied on Jorum for a fact, that is that
14 cold allodynia and hyperalgesia are frequent clinical findings in patients
15 with neuropathic pain, if I recall the Examiner's answer that's the only thing
16 the Examiner cited in Jorum.

17 Does it make any difference that Jorum's kind of therapy doesn't have any
18 relation to what the claimed therapy is? It was just used as a fact reference.

19 MR. CUNNINGHAM: Well, the first sentence in the Jorum abstract
20 indicates that allodynia and hyperalgesia are frequent clinical findings in
21 patients with neuropathic pain. However, Jorum isn't concerned with the
22 same method of treatment used by the inventors using a different compound;
23 and the Examiner has applied Jorum -- basically, for that teaching that
24 frequent clinical findings in patients with neuropathic pain include the
25 symptoms of allodynia and hyperalgesia.

1 Jorum wasn't relied on for teaching treatment of these particular symptoms,
2 but even if it were, it's using a completely different drug and class of
3 chemical compounds to treat those symptoms.

4 JUDGE GRIMES: Any more questions?

5 JUDGE FREDMAN: I don't think so.

6 JUDGE GRIMES: Thank you.

7 MR. CUNNINGHAM: Thank you.

8 Whereupon, the proceedings at 2:20 p.m. were concluded.

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